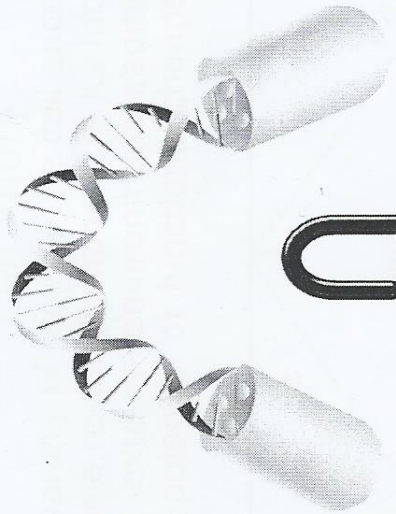
CAPSULE



apsule

Together to cross the 1st pathway

SECOND YEAR

PATHOLOGY REVISION 1

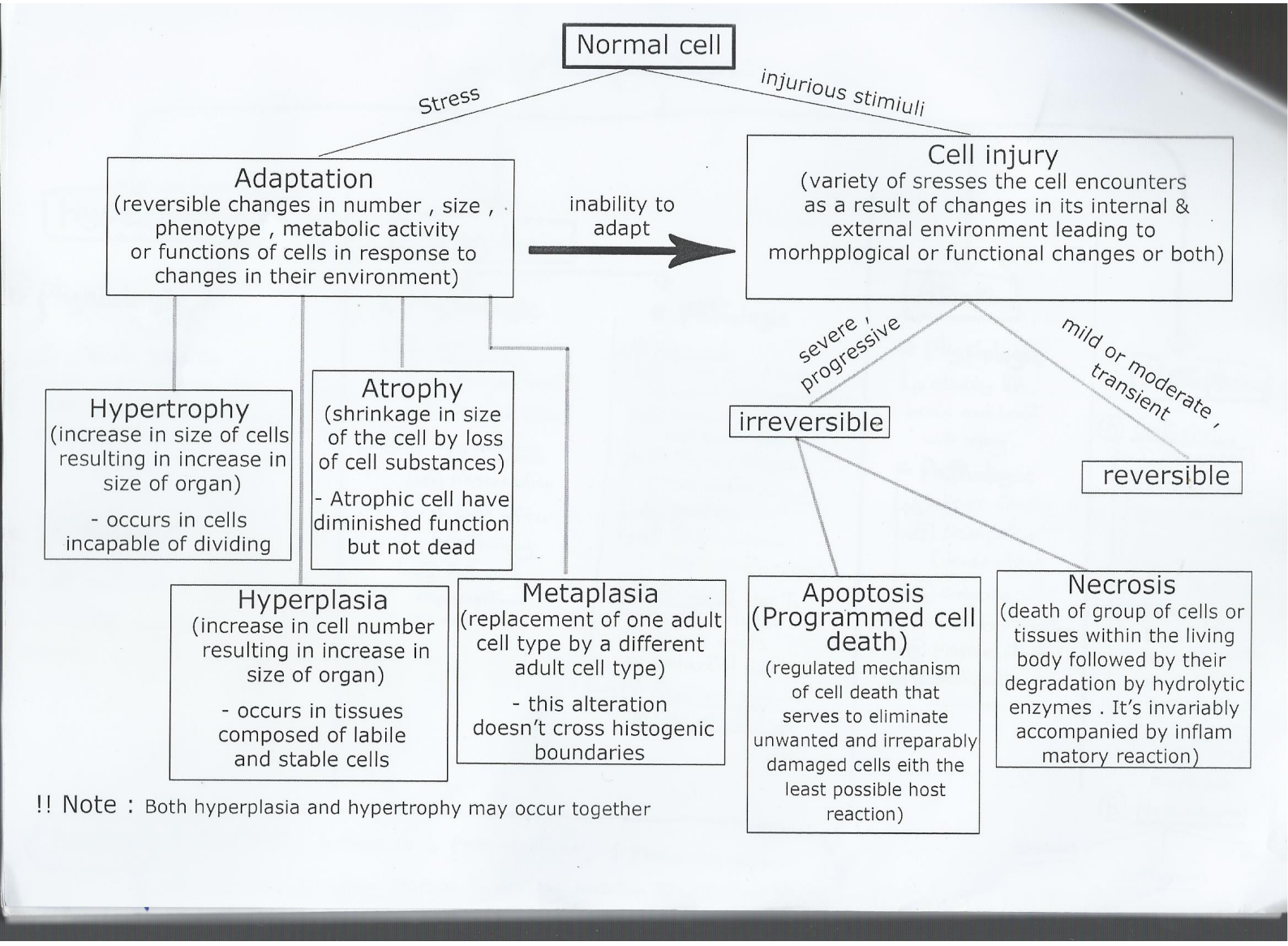
DR . NADIA GALAL (CELL INJURY)

CAPSULE

CAPSULE TEAM

SAHWA FAMILY

CAPSULE



!! Note : Both hyperplasia and hypertrophy may occur together

-: Adaptation :-

Hypertrophy

* **Physiologic**
  - ① Uterine smooth muscle in pregnancy (accompanied by hyperplasia)
  - ② Skeletal muscles in atheletes.
* **Pathologic**
  - Left ventricular in systemic hypertension and aortic valve disease.

Hyperplasia

* **Physiologic**
  - ① Hormonal
    - ⓐ Female breast
    - ⓑ Pregnant uterus
  - ② Compensatory
    - ⓐ Regeneration of Liver after hepatectomy
    - ⓑ Following nephroectomy on one side
* **Pathologic**
  - ① Hormonal
    - ⓐ fibrocystic disease of breast (estrogen excess)
    - ⓑ endometrial (estrogen excess)
    - ⓒ Thyroid (Goiter) (TSH excess)
    - ⓓ prostatic
    - ⓔ Bone marrow (erythropoietin excess)
  - ② Epithelial due to Chronic irritation
    - Brunn's nests in bilharzial cystitis
  - ③ Reactive lymphoid in case of infection

Atrophy

* **Physiologic**
  - atrophy of brain and heart with aging.
* **Pathologic**
  - ① disuse atrophy
  - ② Neuropathic (denervation)
  - ③ endocrine: Loss of its stimulation
  - ④ Pressure atrophy
  - ⑤ inadequate nutrition

Metaplasia

- Ⓐ Epithelial
  - ① Squamous
    - From pseudo-stratified Columnar Ciliated epithelium (in bronchi, in nasal polypi and rhino scleroma
    - From simple Columnar epith. (endocervix, gall bladder)
  - ② Columnar
    - in barret's esophagus
- Ⓑ Mesenchymal
  - osseous
  - Cartilaginous
  - Myeloi

Notes

① In Atrophy → there is ↓ Protein synthesis, ↑ Protein degradation.

② Metaplasia is often response to chronic irritation to withstand stress.

Cell injury

Causes

- Genetic defects
- Aging
- Nutritional imbalances
- Immunologic reaction
- Infectious agents
- Chemical agents
- Physical agents
- O_2 deprivation (Hypoxia & ischemia)

Pathogenesis

A) The type of injury, its duration and its severity

B) The Type, status, adability and genetic Makeup of Cell injury

* Striated muscle (skeletal muscle) withstands ischemia for 2-3 hours but Cardiac muscle dies after only 20-30 minutes.

Note: although there are no definitive morphological or biochemical Correlates of irreversibility but there are 2 Phenomena characterize
- Mitochondrial dysfunction
- disturbance of mem. function

Mechanism

1. Depletion of ATP
2. Damage of Mitochondria (site of ATP Synthesis)
3. Influx of Calcium
4. accumulation of O_2 derived free radicals (oxidative stress)
5. Defects in membrane Permeability (membrane damage)
6. Damage to DNA & proteins genetic apparatus of Cells (nuclear damage)

Mechanisms

* اقلب الصفحة لتلاقي مراجعة سريعة على الـ

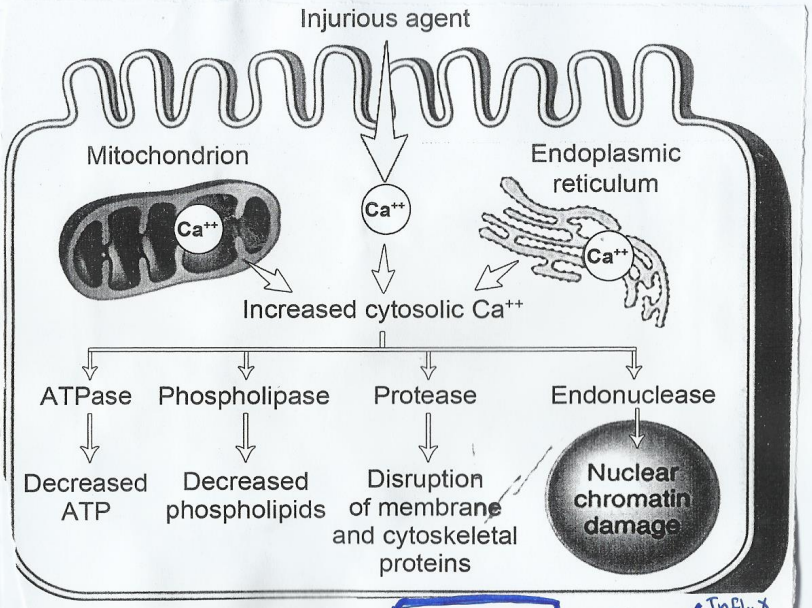


Fig. 2.10: Effects of increased cytosolic calcium in cell injury (Influx of Ca)

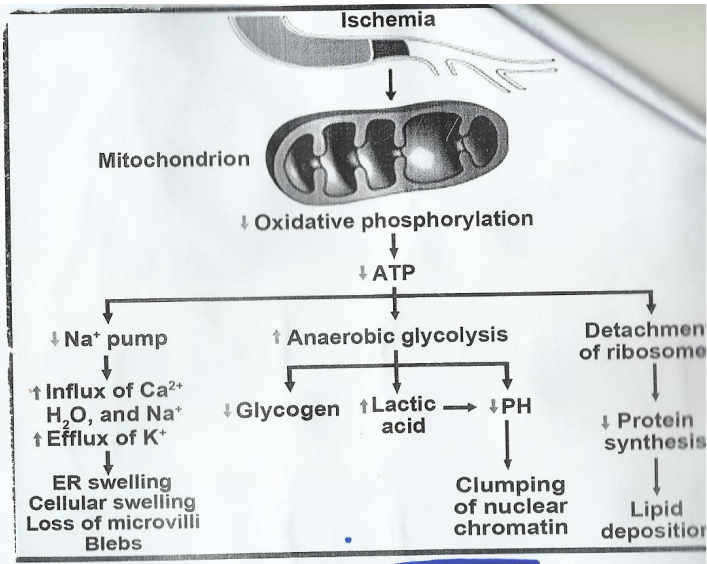


Fig.2.9, Effects of ATP depletion

Pathological effects ROS:

Fatty acids → oxidation → generation of lipid peroxidases → disruption of Plasma membrane
Proteins → oxidation → loss of enzymatic activity, abnormalfolding
DNA → oxidation → mutations.

Fig. 2.11: Pathological effects of accumulation of oxygen-derived free radicals

ATP depletion
influx of Ca
oxidative stress
لهم السبب فإنه يصل :
nuclear damage
Membrane damage
Mitochondrial damage
v. Imp.
Nuclear damage
Pyknosis → Condensation and clumping of protein, dark, basophilic
karyorrhexis → Nuclear fragmentation into small bits.
Karyolysis
Dissolution of nucleus

Types of Cell injury

reversible

Morphology

A) Hydropic change
- accumulation of water
- Pathogenesis: Imparied regulation of Na & K
  - ↓ ال Na بيدخل الخلية وبيدخل معاه ال water
- Grossly: organ → Pale → ↑in weight
- Microscopically → Small clear vacuoles within cytoplasm.

B) hyaline change

C) Mucoid change

irreversible

Necrosis
- **Def.** → ف أول ورقة ف المراجعة والتعريف مهم جداً.
- Morphology: More eosinophilic, nuclear changes
- **Types** ⇐ مهم جداً (فيه ف آخر المحاضرة التانية أبقى ستوفرها)

Coagulative
- EX: infarction heart, spleen, Kidney
- grossly: Pale yellow, Swallen, firm, opaque
- Microscopically: Dead Cells with Preserved basic tissue architecture but details (nuclei) are lost.

Liquefactive
- EX: infection in brain, Pyogen abscess, Amoebic abs.
- grossly: turbid fluid > leaves Cavity (cyst)
- Micro: Creamy white Pus, there's Cyst

Caseous
- EX: TB
- grossly: friable yellow white, look Like cheese or casein of milk
- Micro: Complete Loss of tissue architecture

Fat
- EX: breast trauma, Acute Pancreatic necrosis
- grossly: opaque white, Calcification, chalky white masses
- Micro: giant Cells, dead cells.

fibrinoid
- EX: Vasculitis, Polyanteritis nodosa, Malignant hypertension.
- grossly: bright pink & amorphous
- Micro: eosinophilic, hyaline

apoptosis
- Karyolysis
- Karyorrhexis
- Pyknosis

Apoptosis

Def.
(ن أول ورقة ن الراجعة)

Types

- **Physiologic**
  - during embryogenesis
  - Cells of hormone dependent tissues e.g. endometrial shedding, regression of lactating breast
  - Thymus in early age
- **Pathologic**
  - in tumors exposed to chemotherapeutic
  - in graft rejection
  - in viral hepatitis (Councilman apoptotic)
  - in prostatic atrophy
  - in radiation & hypoxia
  - in degenerative disease of CNS e.g. Alzheimer

Pathological features

Morphology

- Cytoplasm: more eosinophilic
- Cells: shrinked (mummified)
- nucleus: Pyknosis or karyorrhexis
- Cell membrane shows Projections
- formation of apoptotic bodies
- No inflammatory reactions
- apoptotic bodies are phagocytosed by Macrophages

Mechanism

(2) Mitochondrial intrinsic Pathway
- P53 → stim. of apoptosis
- Bcl-2 → inhibition of apoptosis

(1) death receptor extrinsic Pathway
- FAS → stimulation of apoptosis

Stimu. of apoptosis

* Caspases → activate nucleases → degrade DNA
* Caspases & other enzymes → destroy nucleoproteins & cytoskeletal Proteins

(6)

(V.V.V. imp.) **Table 2.1: Difference between Apoptosis and Necrosis**

Death of individual cells — Death of group of cells

Feature	Apoptosis	Necrosis
Definition	Programmed and coordinated cell death	Cell death with degradation of tissues by hydrolytic enzymes
Causes	Physiologic and pathologic processes	Pathological, hypoxia, toxins,..
Morphology	1. No inflammatory reaction 2. Death of single cell or small clusters of cells 3. Cell shrinkage 4. Cytoplasmic blebs on membrane 5. Apoptotic bodies 6. Chromatin condensation 7. Phagocytosis of apoptotic bodies by macrophages.	Inflammatory reaction present Death of many adjacent cells Cell swelling initially Membrane disruption Damaged organelles Nuclear disruption Phagocytosis of cell debris by Macrophages
Molecular Changes	1. Lysosomes and other organelles intact 2. Controlled by hormones and enzymes (FAS, BCL-2, p53) (Stimu. Stimu. Inhib. Stimu.)	1. Lysosomal breakdown with liberation of hydrolytic enzymes 2. Cell death by ATP depletion, membrane damage, free radical injury.

خلايا الجسم بيعمل responses تانية وتؤدى إلى Cell injury برضه *
- → gangrene
- → intracellular accumulations
- → Pathologic Calcification
- → Cell aging

Gangrene

Def.
(is necrosis (usually Coagulative) of tissue with superadded Putrefaction)

Types

Gas
- Site: wounds, Musle, Colon
- Causes: gas Forming bacteria (gram +ve anerobic bacteria)

Dry
- Site: distal part of a limb due to ischemia
- Causes:
  - → Atherosclerosis
  - → Thromboangitis obliterans (Buerger's disease)
  - → Raynaud's disease, ergot Poisoning
  - → Trauma
- evolution: there are line of demarcation, Line of separation
- grossly: dry, shrunken, dark black
  - haemolysed RBCs → iron + H_2S → black

Wet
- Site: Moist tissues & organs as intestine, lung, Mouth
- Causes:
  - → Strangulated hernia
  - → valvus
  - → intussuscepation
  - → Mesentric vascular occlusion
  - → diabetic foot
  - → bed Sores
- evolution: abdominal pain, apsolute Constipation, No line of demarcation

Table 2.2: Difference between of Dry and Wet Gangrene

Feature	Dry Gangrene	Wet Gangrene
Site	Commonly limbs	More common in bowel, lung
Mechanisms	Arterial occlusion	More commonly venous obstruction, less often arterial occlusion
Grossly	Dry, shrunken and black	Moist, soft, swollen, rotten and dark
Putrefaction	Limited due to very little blood supply	Marked due to stuffing of organ with blood
Line of demarcation	Present at the junction between healthy and gangrenous part	No clear line of demarcation
Bacteria	Bacteria fail to survive	Numerous
Prognosis	Generally better due to little toxemia	Generally poor due to profound toxemia

Intracellular accumulations

Defi.

↳ (accumulation of substances in abnormal amount can occur within the cytoplasm (especially lysosomes) or the nucleus of the cell)

- if mild → reversible cell injury
- if severe → irreversible cell injury

divided into

- increase amount of normaly present sub. due to excessive Metabolism e.g. → Lipids, Proteins, carbohydrates
- increase amount of abnormally present sub. due to abnormal Metabolism e.g. Lipid storage disease
- Pigments

Fatty change in liver

(accumulation of neutral fat (triglycerides) within cytoplasm of Parenchymal cells)

Grossly: size: enlarged
Consistency: Soft
Edge: rounded
Cut surface: bulging, yellow, greasy

Micro: Clear vacuoles (Signet ring)

Causes:
- Hyperlipidemia in (obesity, diabetes, Congenital)
- alcoholic Liver
- starvation in Malnutrition, hypoxia, hepatotoxins.

Pathogenesis (lipid metabolism)

Free fatty acids
α-glycero-phosphate + fatty acids + acetate
Fatty acids → oxidation to ketone bodies, phospholipids, cholesterol esters (Catabolism)
Fatty acids + Apoprotein → triglycerides → Lipoprotein → Lipid accumulation

Pigments

(Colored substances that are exogenous (from outside body) or endogenous (within body itself))

endogenous Pigments

- Melanin
- Haemoprotein derived Pigments (haemosiderin)
- Lipofuscin (wear and tear Pigment) (yellowish brown pigment)

exogenous Pigments

- inhaled Pigments (Carbon)
- injected pigments (Tattooing)

Pathologic Calcification

Def.

→ (deposition of Calcium Salts in tissues other than osteoid or enamel is called Pathologic or heterotropic Calcification)

Pathogenesis

→ Inorganic phosphate binds with Ca ions
↓
Calcium phosphate

Types

Dystrophic

→ Normal Ca level (9-11 mg%)
→ deposition on abnormal tissue
→ Causes:
  → ① in dead tissue
    → Necrosis (Caseous, Liquefactive, fat, Coagulative)
    → Thrombi
    → Haematomas
    → in breast Cancer
    → Dead parasites (hydatid cysts and shistosoma eggs
  → ② in denegenrated tissues
    → old scars
    → Atheroma
    → Monckeberg's sclerosis in tunica media of muscle.

Metastatic

→ increased Ca level
→ deposition on normal tissue
→ associated with deranged Ca metabolism & hypercalcemia
→ Causes: Ⓐ eXcessive mobilization of Ca from bone
  → Hyperparathyrodism
  → bony destructive lesions
  → Prolonged immobilization
  Ⓑ eXcessive absorption of Ca from gut
  → Hypervitaminosis D
  → Milk alkali syndrome
  Ⓒ Vitamin D related disorders (vit. D intoxication & Sarcoidosis)

Feature	Dystrophic calcification	Metastatic calcification
Definition	Deposits of calcium salts in dead and degenerated tissues	Deposits of calcium salts in normal tissues
Calcium metabolism	Normal	Deranged
Serum calcium level	Normal	Hypercalcemia
Causes	-Necrosis (caseous, liquefactive, fat, coagulative) -Thrombi, hematoma. -Dead parasites, old scars -Atheroma, -Monckberg's sclerosis -Certain tumors	-Hyperparathyroidism -Bony destructive lesions -Prolonged immobilization -Hypervitaminosis D -Milk-alkali syndrome -Sarcoidosis
Pathogenesis	Increased binding of phosphates with necrotic and degenerated tissue, which in turn binds to calcium forming calcium phosphate precipitates.	Increased precipitates of calcium phosphate at certain sites due to hypercalcemia e.g. in kidneys, lungs, stomach, arteries, synovium.

Questions

دى أسئلة جديدة متنساش ترجع على الأسئلة اللي فاتت الي حطيناها أثناء المحاضرات

* Choose:

1) Enzymatic fat necrosis occurs in:
a) fat embolism b) Tuberculous peritonitis
c) Acute haemorrhagic pancreatitis d) Gas gangrene e) Non of the above

2) Fragmentation of nuclei in necrotic cells is called
a) Pyknosis b) karyolysis c) karyorrhexis d) Autolysis e) None of the above

3) Fatty change occurs in:
a) Liver b) heart c) kidney d) All of the bove c) None of the above

4) infarction of the kidney is example of
a) Caseating necrosis b) fibrinoid necrosis c) fat necrosis d) Liquefactive necrosis
e) Coagulative necrosis.

5) Concerning apoptosis, it's:
a) programmed cell death b) energy dependent process c) No inflammatory Rx
d) individual cell necrosis e) all of the bove

6) Reversible cell injury is characterized by:
a) Nuclear changes as pyknosis b) Pathological calcification
c) formation of apoptotic cells d) accumulation of sodium and water inside cell.
e) None of the above

7) A biopsy from the liver shows that all liver cells are vaculates and nucleus is giving what is called (signet ring). The cause is:
a) Hypoxia, b) Starvation c) Carbon tetrachloride poisoning d) diabetes mellitus e) all the above

8) Which of following pathologic changes would be considered irreversible:
a) hydropic vacuoles b) karyorrhexis c) fatty change
d) Mitochondrial swelling

9) Fat can be seen in frozen sections by one of the following stain:
a) Methyl violet b) Toluidene blue c) Sudan III
d) Congo red

10) Caseation necrosis is most characteristic of:
a) acute myocardial infarction b) Tuberculosis
c) Acute pancreatitis d) brain infarction
e) Pulmonary pneumoconiosis

11) The following is/are seen in cells undergoing necrosis:
a) increase in DNA synthesis b) fatty change
c) Both a & b d) Neither a nor b

* True or False

1. Hydropic change is an exaggerated form of Cellular Swelling (✓)
2. Apoptosis is only a physiological process (✗)
3. Fatty change is abnormal accumulation of Lipoprotein in Parenchymal Cells (✗)
4. irreversible Cell injury leads to Swelling of Cells due to failure of Na pump (✗)
5. Fatty change is abnormal accumulation of triglycerides in parenchymal Cells (✓)

عشان المراجعة تكون مع حاول تذاكر الأول أو على الأقل تقرأ المنهج وبعد كده امسك المراجعة وتذكر.
(إن الله لا يضيع أجر من أحسن عملاً)

Note

* Cases :-

1. A 38-year old man has a health screening examination. He has a routine chest X-ray that shows a 2cm nodule in the right lower lobe. The nodule has focal Calcifications. A wedge resection of the nodule is done. on Microscopic examination the nodule shows Caseous necrosis and Calcification. which of the following processes explain appearance of Ca deposition ?

a) Dystrophic Calcification b) Apoptosis c) hyperCalcemia d) Metastatic Calcification e) excessive ingestion of Ca

2. In an experiment, a glass bead is embolized to a branch of renal artery. A day later there's a focal area in which the renal parenchymal cells in the distribution of the occluded artery show karyolysis and karyorrhexis. The outlines of cells are still visible, but the nuclei have lost basophilic staining and the cytoplasm is eosinophilic but Pale. What type of necrosis most likely present?

a) liquefactive necrosis b) fat necrosis c) Caseating necrosis d) Coagulative necrosis e) fibrinoid necrosis

#Capsule ....

تم بحمد الله #